

# The baby at risk of HIV

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# Outline of the Presentation

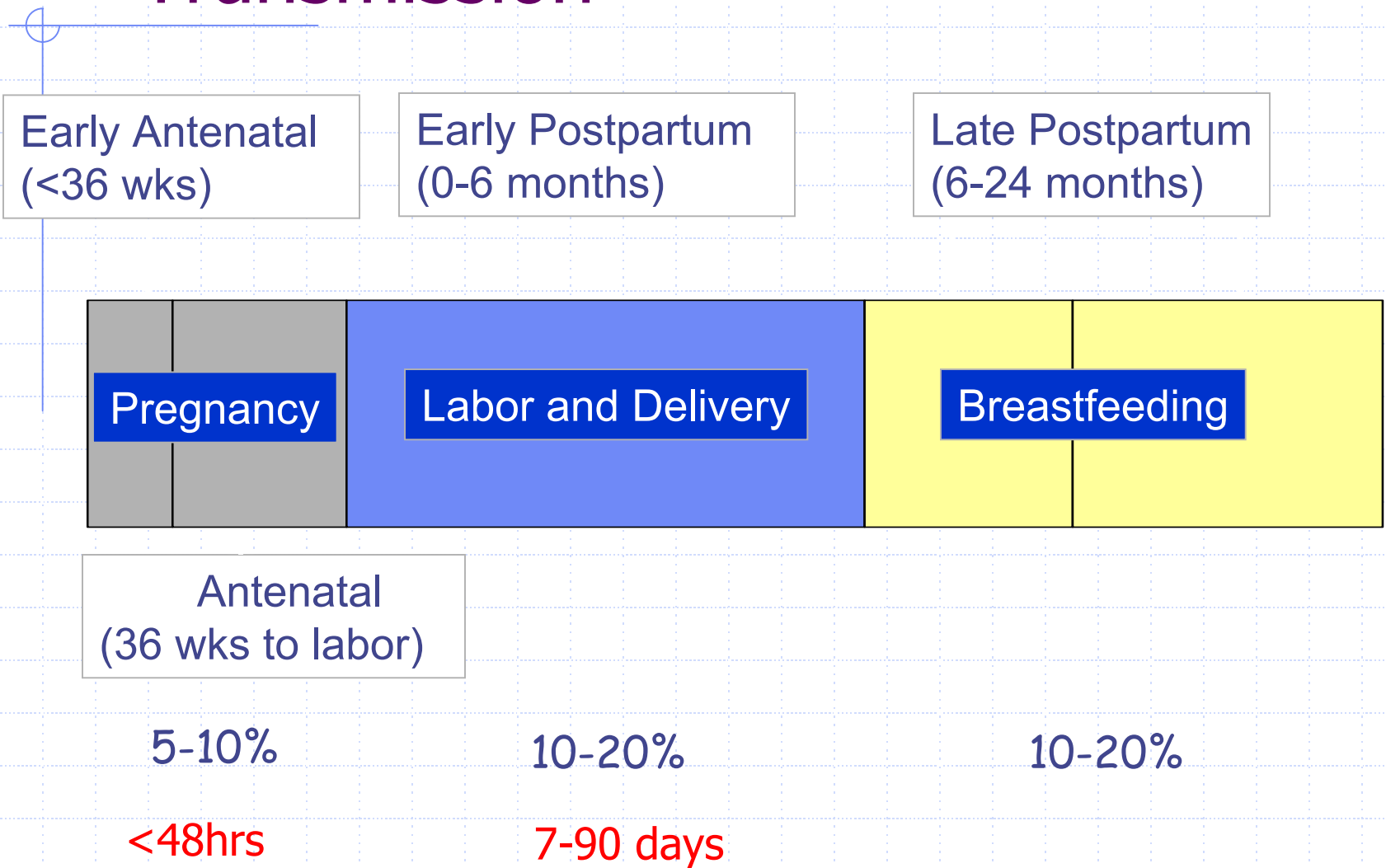
◆ Overview

◆ Review of evidence on risk factors

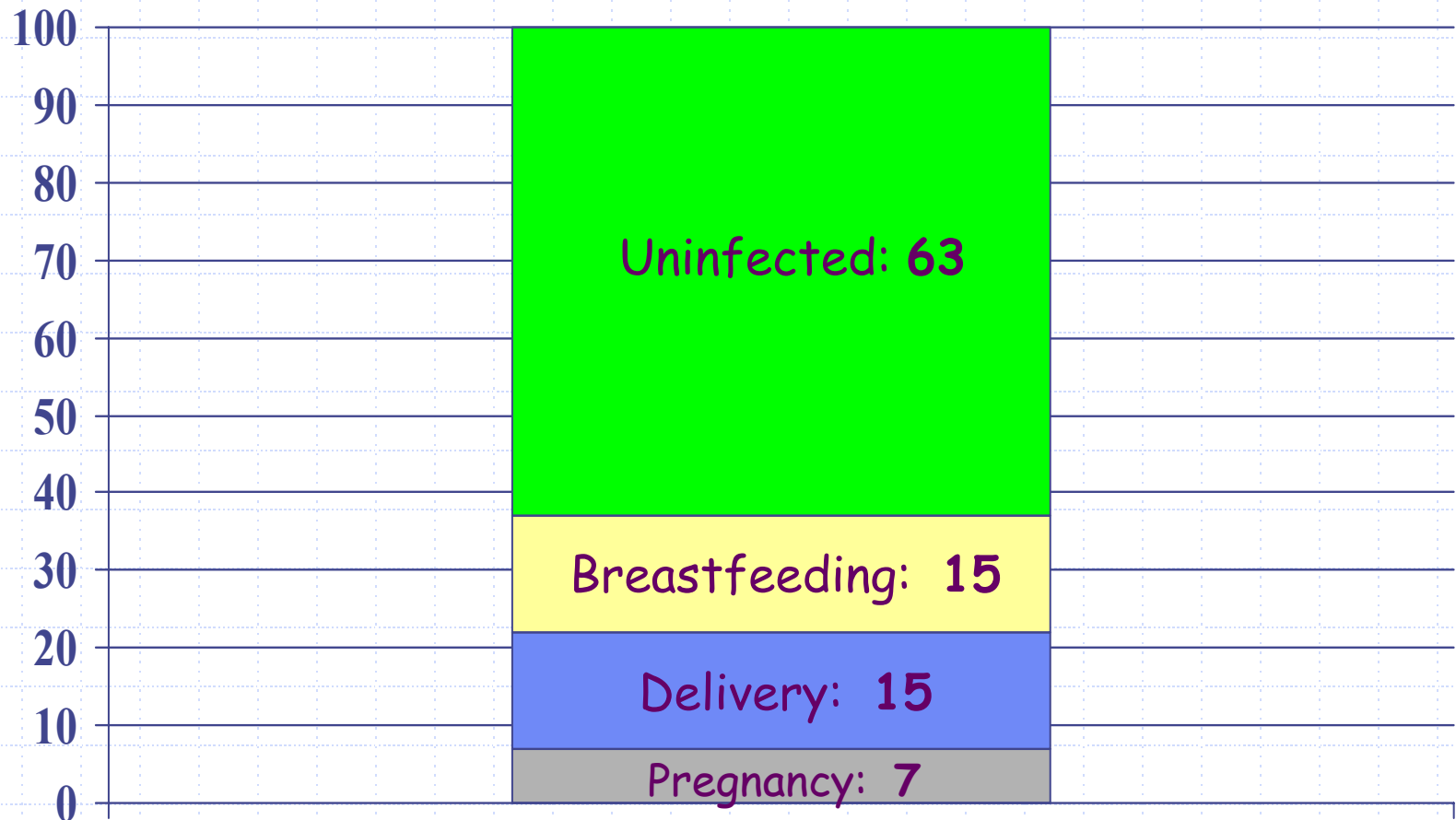
# HIV Transmission Efficiency Rates

Type of Exposure	Efficiency of single exposure
Blood Transfusion	> 95%
Vertical Transmission	30% (12-40)
Breast Milk	14-20%

# Timing of Mother-to-Child Transmission



# MTCT in 100 HIV+ Mothers by Timing of Transmission



# Risk Factors for HIV Transmission



# Maternal Risk Factors For Transmission of HIV

- ◆ Immune/health status
- ◆ Plasma viral load
- ◆ Placental factors
- ◆ Breast milk virus
- ◆ Breast inflammation (mastitis, abscess, bleeding nipples)
- ◆ New HIV infection
- ◆ Viral Characteristics

# Placental Risk Factors for transmission of HIV

- ◆ Transmission may occur through an intact placenta by transcytosis
- ◆ Risk increases if placental is damaged i.e. chorioamnionitis, smoking
- ◆ Usually in last trimester due to materno - fetal transfusion



# Risk factors for Intrapartum Transmission

- ◆ First born twin
- ◆ Vaginal Delivery
- ◆ PROM > 4 hrs
- ◆ Difficult labor, Instrumentation
- ◆ Genital Infection
- ◆ Fetal Scalp Electrodes

# Infant Risk Factors For Transmission of HIV

- ◆ Non-exclusive BF
- ◆ Age (first months)
- ◆ Lesions in mouth, intestine
- ◆ Infant immune response

# Maternal viral load

- ◆ Indirect evidence of advanced maternal disease
- ◆ Important predictor of **intra-partum MTCT**  
(Leroy et al, 2001; Semba et al, 1999)
- ◆ Risk factor during **breastfeeding**
- ◆ The threshold below which there is no risk has not been identified

Kenya (Richardson et al, 2003), Tanzania (Fawzi et al, 2002), West Africa (Leroy et al, 2003)

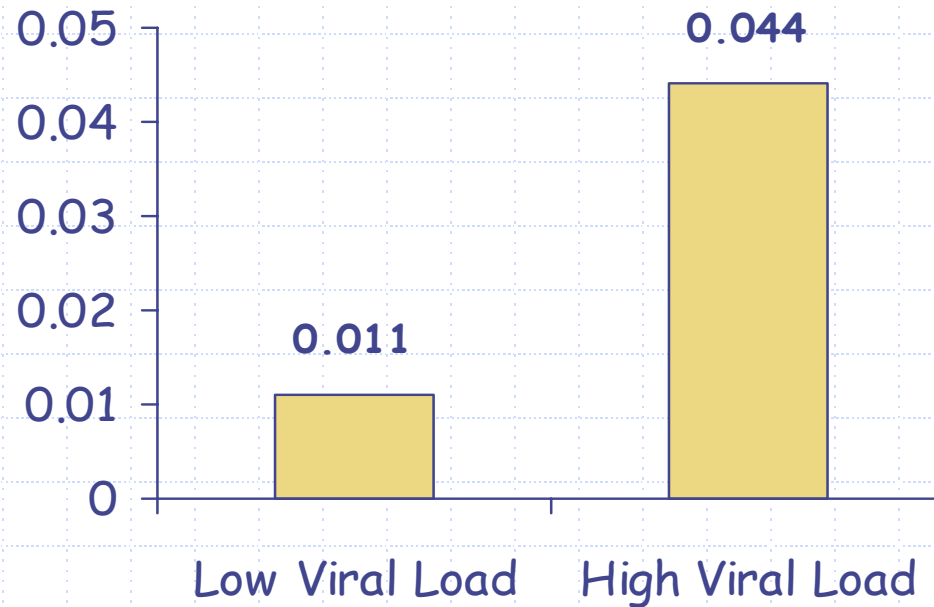
# Maternal Virus Load and Perinatal Transmission

<b>Viral Load</b>	<b>Transmission Rate (%)</b>
< 1000 copies/ml	0
1000 –10000	16.6
10,001-50,000-	21.3
50,001-100,000	30.9
> 100,000	40.6

Garcia BM. NEJM, 1999

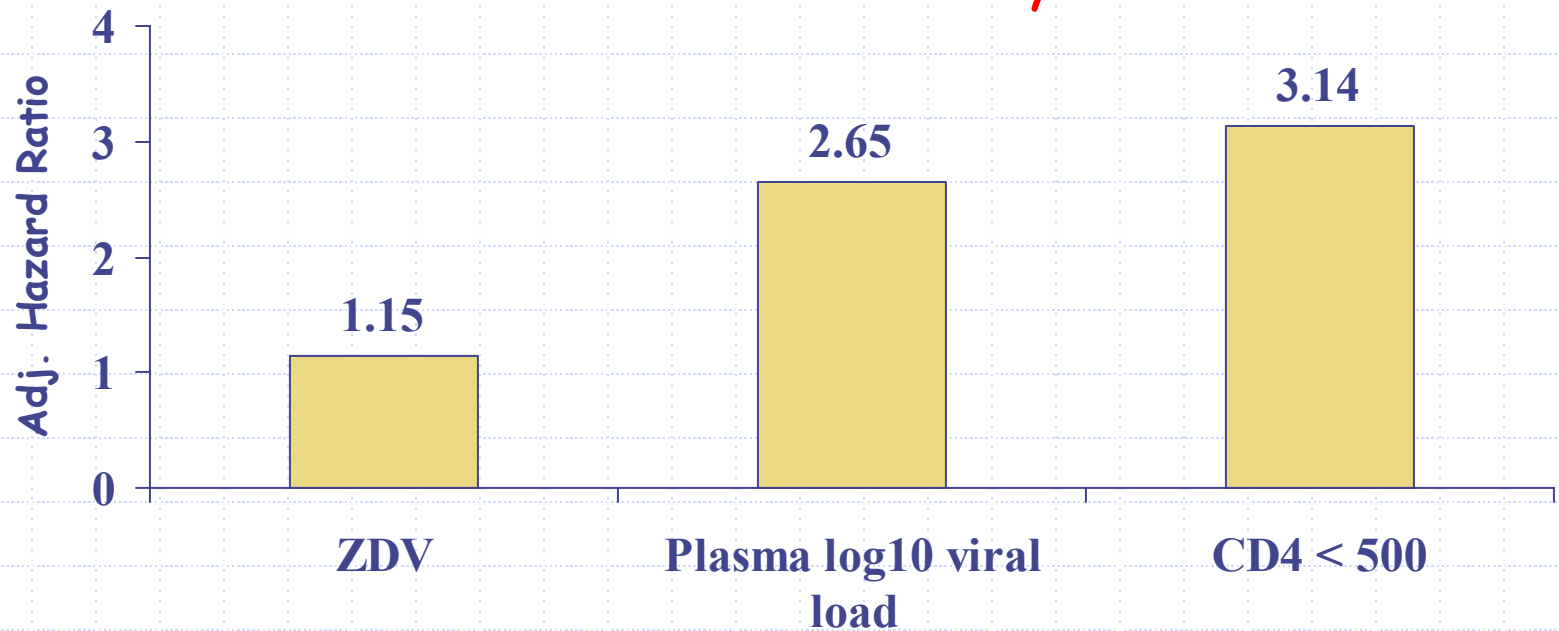
# Maternal Viral Load

Risk of HIV transmission per  
day of BF (%)



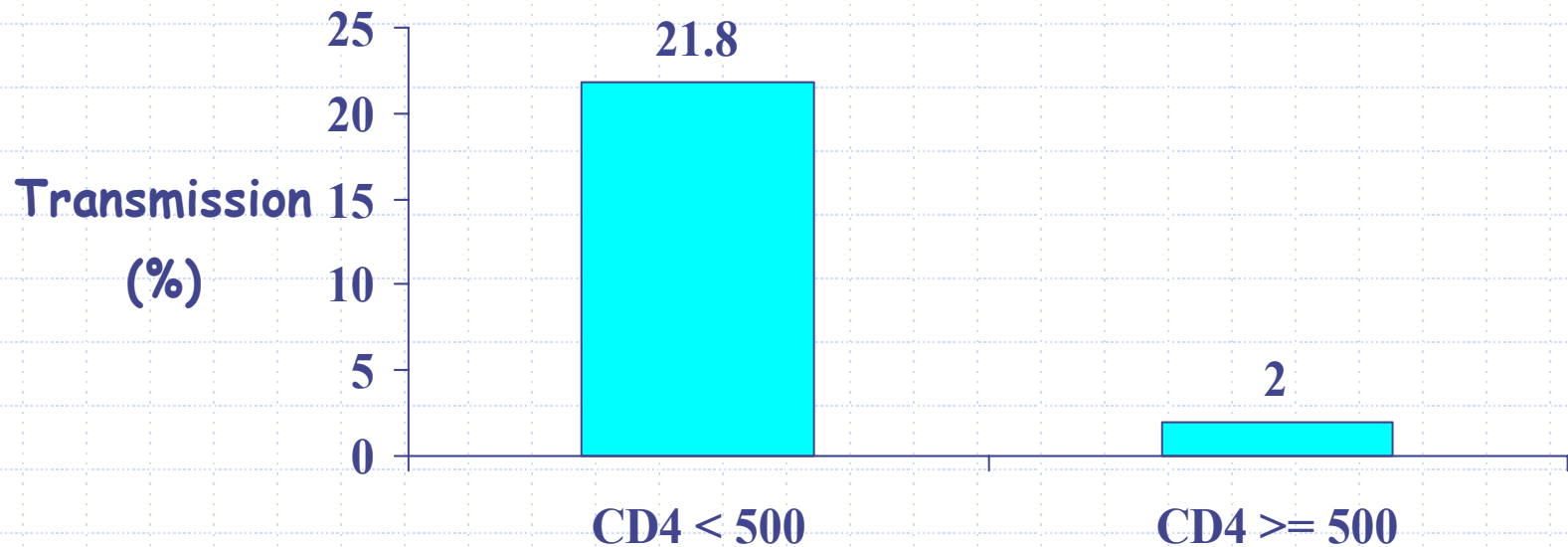
# Maternal viral load

Adjusted HR for Postnatal Transmission in West Africa Combined Analysis



# Maternal immune status

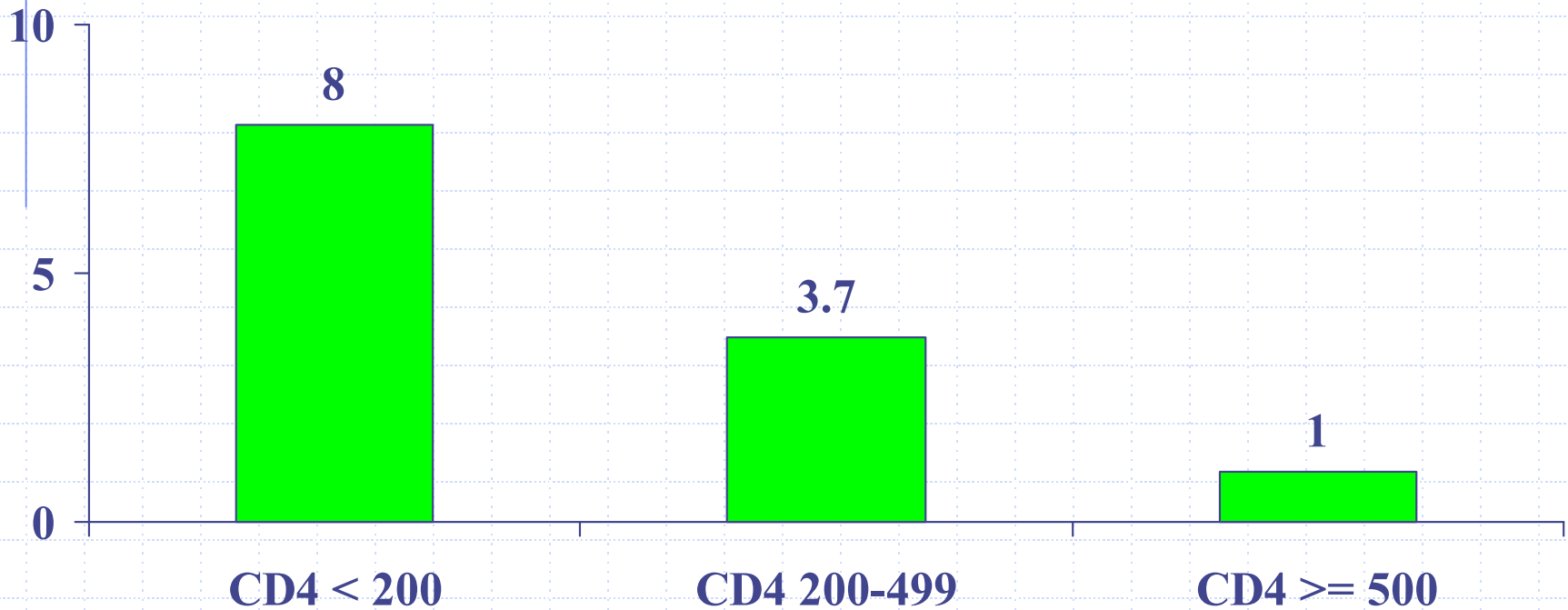
HIV transmission from 6 w - 24 mo in West Africa by maternal baseline CD4



Leroy et al 2003

# Maternal immune status

Hazard ratio for postnatal HIV transmission



BHITS meta-analysis, Read et al (CROI 2003)



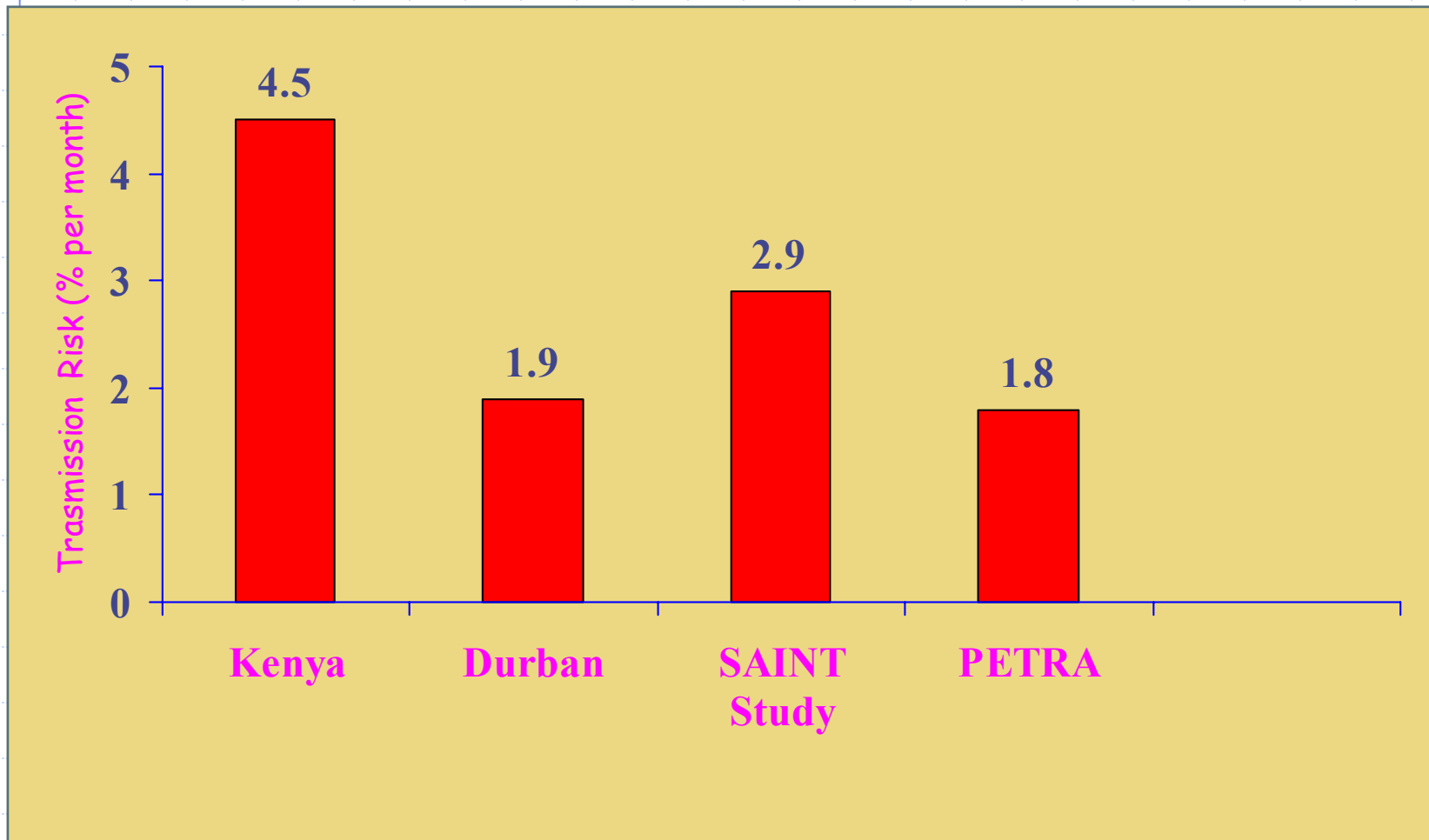
# Neonatal Period

- higher prevalence of mastitis, breastfeeding problems
- infant gut more immature, permeable
- greater exposure (higher concentration of cells)

(Nduati et al, 2000; John et al, 2001)

# Neonatal Period

Estimated postnatal transmission during the first month of life



# Multiple gestation

Mode of Delivery	Twin A	Twin B
Vaginal	50%	19%
Caesarian	38%	19%

Goedert JJ. Lancet 1991;338:1471.

# Breastfeeding and HIV



# How does HIV transmission during breastfeeding occur?

- ◆ Exact mechanisms unknown
- ◆ HIV virus in blood passes to breast milk
  - cell-associated, cell-free virus observed
  - virus appears intermittently (undetectable ~ 25-35%)
- ◆ Virus may also come directly from infected cells in mammary gland
  - produced locally in mammary macrophages, lymphocytes, epithelial cells (Becquart et al, 2002)

# How does HIV transmission during breastfeeding occur?

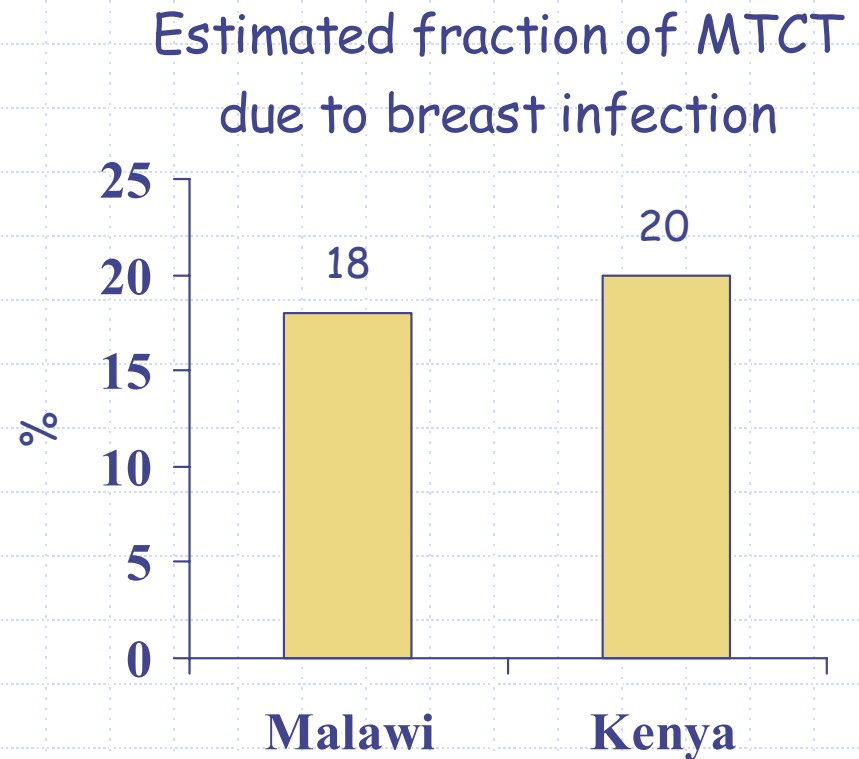
## ◆ **Infant consumes HIV**

- HIV enters/infects infant through permeable mucosal surfaces, lymphoid tissues, and/or lesions in mouth, intestines
- Although BF infant may consume >500,000 virions, >25,000 infected cells per day, majority do NOT become HIV infected (Lewis et al, 2001)

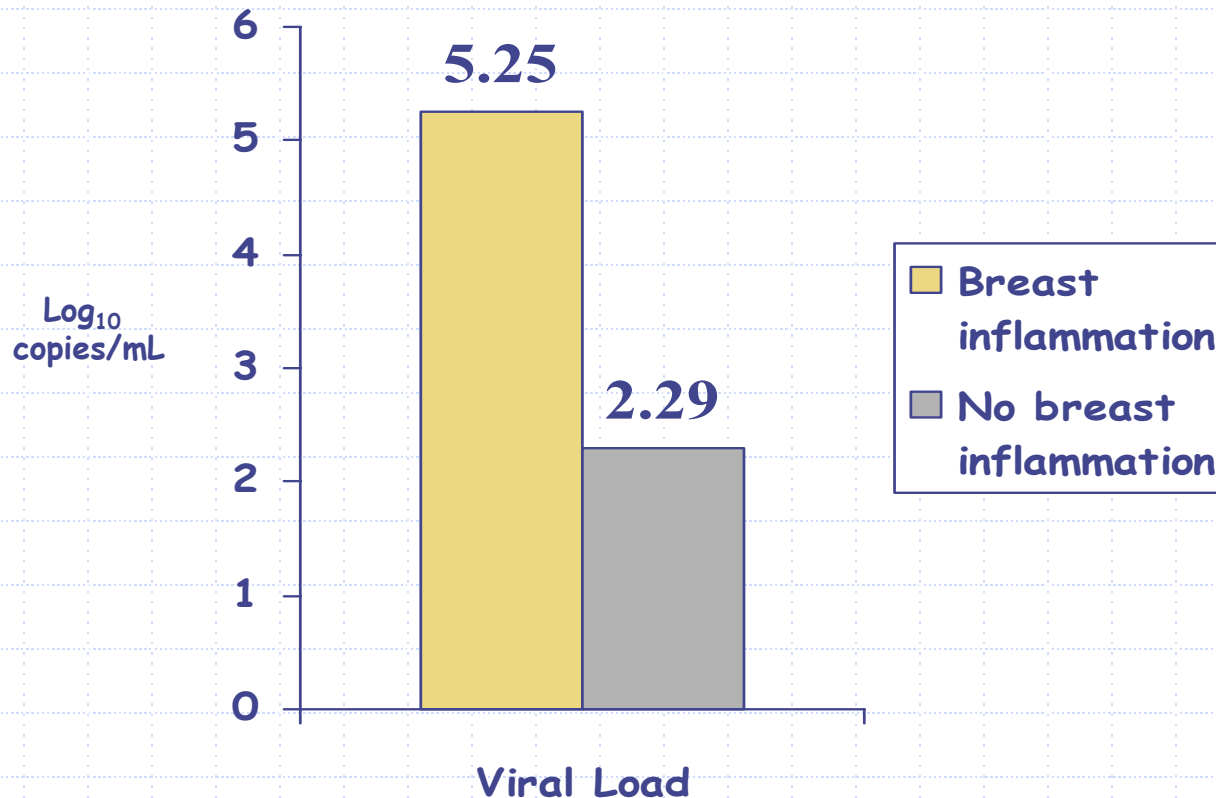
## ◆ **Immune factors** in BM, saliva play a role (Miller et al, 2002; Sabbaj et al, 2002; Farquhar et al, 2002; Van der Perre et al, 1999; 1993; 1988)

# Risk factors for postnatal transmission: Breast Pathology

- ◆ Breast inflammation & mastitis → increased risk of postnatal transmission (Embree et al; John et al; Semba et al)
- ◆ Nipple lesions, breast abscesses → increased transmission (Fawzi et al, 2002; Embree et al, 2000; Ekpini et al, 1997)
- ◆ Sub-clinical mastitis → higher viral load in BM (Willumsen et al, 2000; Semba et al, 1999, Hoffman, 2003)



# Association between breast inflammation and breast milk virus





# Breast Pathology

## Prevalence of breast pathologies in HIV+ women in Africa

### ◆ **Mastitis (clinical or sub-clinical):**

- Clinical exam: 7-11% (Embree, 2000; John et al, 2001)
- Na<sup>+</sup>/K > 1.0: 11-12% at 6, 14 wk (Willumsen et al, 2000)
- Na<sup>+</sup> > 12 mmol/L: 16.4% at 6 wk (Semba et al, 1999)

### ◆ **Nipple lesions:**

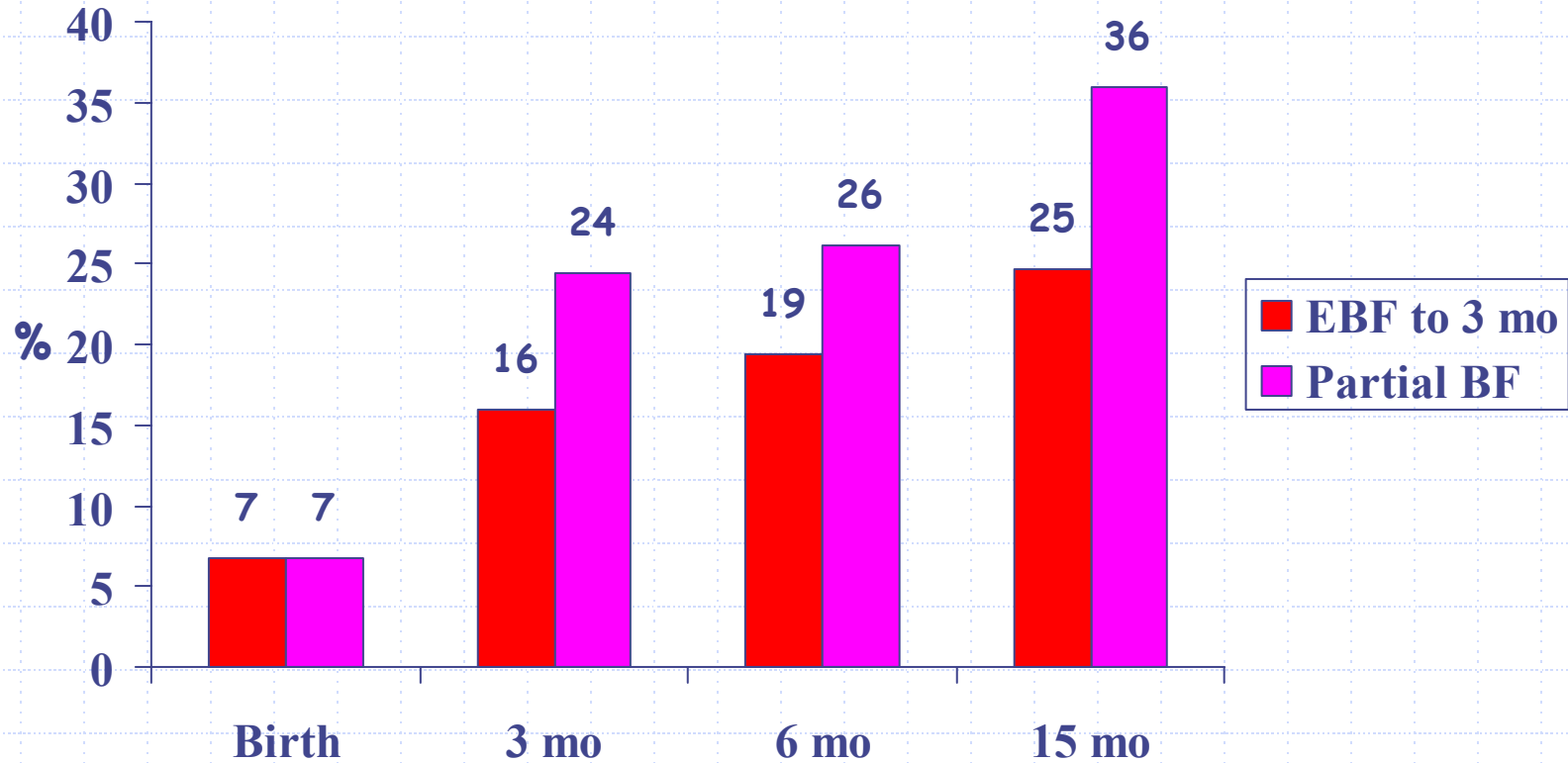
- Clinical exam: 11-13% (Embree, 2000; John et al, 2001)
- Clinical exam: 10% (Ekpini et al, 1997)
- Hospitalized infants: 11% (Kambarami et al, 1997)

### ◆ **Breast abscesses:**

- Clinical exam: 12% (John et al, 2001)
- Clinical exam: 3% (Ekpini et al, 1997)

# Early Mixed breastfeeding

## Cumulative HIV transmission Durban, SA



Coutsoudis et al, 1999; 2001

# Zidovudine Prophylaxis to mother and Rate of Perinatal transmission

TEST Group %	Placebo Group %
7.6 (95% CI 4.3-12.3)	22.6 (95% CI 17-29)

Pediatric AIDS clinical trial group  
protocol 076. NEJM 1994

# Maternal Malaria and MTCT

- ◆ Among women dually infected with malaria and
- ◆ HIV, high-density placental malaria (>10,000 parasites/mL) was associated with
- ◆ increased risk for perinatal MTCT (ARR 2.0)

Ayisi JG, Emerg Infect Dis. 2004 Apr;10(4):643-52

# Conclusions

- ◆ Perinatal Transmission of HIV is preventable
- ◆ Antenatal counseling and testing
- ◆ Prophylaxis
- ◆ Avoidance of various risk factors

In USA, rate of vertical transmission is less than 2%



Thanks !!!!